Docket # 02N-0115
PhRMA (1)

PhRMA

Benefit and Risk
The Balance in Developing Innovative Medicines

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Benefit & Risk: developing innovative medicines

- Pharmaceutical companies' mission
  - To continue developing innovative medicines to save lives, to prevent, cure, or manage diseases, to relieve pain/suffering, and to improve quality of life
  - To bring these products to market with an established safety profile at a reasonable level of certainty acceptable by the FDA and the general medical community
- Consensus of patients, physicians, regulators, and industry to bring maximal benefits with minimal risks
- All medicines have some risk - how to strike the balance?

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Benefit & Risk: principles of risk management

What is risk management and assessment?

- Different definitions are used by regulators, industry, and academia
  - ***Pre-marketing*** can be defined as *risk detection* and *risk assessment or evaluation*
  - ***Post-marketing*** can be defined as risk detection, assessment, evaluation **AND** *risk communication* and *risk minimization*
  - Risk management begins well before product approval
  - Entire spectrum of 'risk management' activities span the life of the drug

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Benefit & Risk: principles of risk management

Analogy: good benefit/risk management like household budget

- Household budget
  - ***No planning ahead - surprises occur***
    - Greater risk for cost overruns
    - Can be costly and painful to manage cost overruns (refinancing debt, home equity loans, austere budgeting, credit card management, etc.)
  - ***Planning ahead - minimal surprises***
    - Lesser risk for budget overruns
    - When cost overruns occur, tend to be lesser in magnitude and easier to manage

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Benefit & Risk: principles of risk management

Analogy: good benefit/risk management like household budget

- Risk management
  - ***No planning ahead - surprises occur***
    - Greater risk for unanticipated safety issues to arise
    - Difficult to manage (labeling changes, mandated studies, restricted use, product withdrawal)
  - ***Planning ahead - minimal surprises***
    - Proactive studies carried up front
    - Signals from clinical trials are followed up and quantified
    - Proactive design of post-marketing surveillance studies
    - Safety issues minimized and easier to manage

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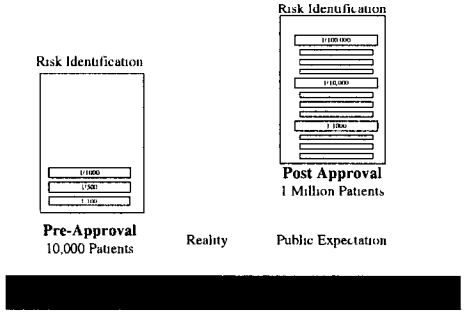
Risk Identification Pre- & Post- Approval

Public expectation of risk knowledge at approval is greater than reality



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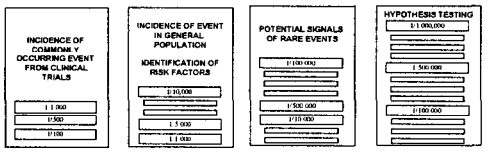
Building Risk Knowledge Base

Post-approval experience allows for identification of smaller risks

Background Epidemiology	Spontaneous Reports	Observational Studies	Other Activities



Risk Management/Assessment Strategy

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Benefit & Risk: principles of risk management

Need to tie risk management tools to a formal process

- Surveillance is the responsibility of all companies
  - Onus is on manufacturer to collect complete, targeted information on adverse events
- Partnership with regulators is critical
  - Reach consensus on areas of risk, as well as plans for assessment and communication of risk
  - Agreement on the development of tools
  - Goal is to minimize surprises
- Any guidelines should be based on tested systems
  - Variations in approaches across products

Collective effort in establishing public health policy - PDUFA III

- Define the risk management 'tools' and their relative strengths & limitations
- Develop risk management plans for each new product
  - Review known epidemiology, carry out incidence & prevalence studies
  - Identify risk areas
    - Assess clinical trials limitations & disease epidemiology
    - Post-approval observational trials confirmation of safety profile
    - Targeted post-approval clinical program refinement of concerns
    - Spontaneous reports rare event identification
  - What additional work needs to be done to assess risk
- Formal FDA concurrence with plan
  - Interpretation of algorithms and outputs
  - Annual re-review of scope

PhRMA (4)

Industry at the Cutting Edge

- Identifying new and novel approaches
  - Automated databases
    - Rapid access to large populations
    - Support to keep valuable database resources available
    - Used by industry, regulatory agencies, and academia
  - Pregnancy Registries
    - Industry at the forefront of their development and use
    - Multi-company support of key registries (anti-epileptic & anti-viral registries)
    - Help in warning women of risks and provides input into physician counseling
- Need to ensure use of systematic approachs to managing risk for physicians, pharmacists, and nurses (cannot have multiple, complex programs to juggle)

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